

**IN THE UNITED STATES PATENT AND TRADEMARK OFFICE**

In re Application of : Dominick A. Cataldo, *et al.*  
Serial No. : 10/816,095  
Filed: : April 1, 2004  
For: : Use of Colloidal Clays for Sustained Release of  
Active Ingredients  
TC/AU : 1615  
Examiner : Neil S. Levy  
Attorney Docket No. : BGT 2-007

HONORABLE COMMISSIONER FOR PATENTS  
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Sir:

Declarant, Dominic A. Cataldo, does declare and state that:

1. I have a B.S. degree from The Ohio State University, Columbus, OH, Major-Anatomy/Microbiology, 1966; M.S. from the University of Dayton, Dayton, OH, Major-Biochemistry/Physiology; and Ph.D. from Yale University, New Haven, CT, Major- Biochemistry/Physiology.
2. My work history is set forth on the summary CV, attached hereto and made a part hereof.
3. I am a co-inventor of and co-applicant in the above-identified application.
4. I am familiar with the Kodama, Van Voris, and Knudson references cited in rejecting the claims in the above-identified application.
5. Pre-forming the colloidal clay adsorbed with pest control agent when both are heated and such pre-form dispersed (coated) with polymer will provide a longer life span for such pest control agent versus dispersing the colloidal clay adsorbed with pest control agent in a polymer coating.
6. In order to demonstrate this, the following tests were conducted by me and/or under my direct supervision and control:

## **EXAMPLE**

### **INFLUENCE OF MIXING TEMPERATURE ON RELEASE OF PESTICIDES FROM SELECTED SORBENTS**

#### **Method**

We placed a liquid thiocarbamate pesticide neat, ENDT (trade name Eptam), chemical formula  $[(CH_3)_2CH]_2N-CO-SC_2H_5$  onto 2 each #42 Whatman filter disks placed into 6-cm open top Al weigh boats, to allow for even distribution and surface area of the sorbed liquid. The selected sorbents were I.30P, I.44PA, and I.34T (these were organically modified with octadecyl ammonium, methyl dihydroxyethyl tallow ammonium, and methyl tallow bis-2-hydroxyethyl hydrogenated-tallow ammonium salts, respectively). They were loaded at room temperature (22°C) and slowly mixed with 98.7% Eptam to a point where loading (33-35% w/w) did not cause the commercial nanoclays to coalesce significantly, but remained friable and a loose powder. Loaded clay samples were placed into 6 cm diameter weigh boats, and held for 18 hrs in enclosed containers, to allow for equilibration of the clay with the active. Loaded-clays uniformly covered the bottoms of the boats to a depth of approx 2-3 mm, to maximize release surface area.

The samples were placed into a 2 L sealed container, having an inlet port and outlet port. Dry nitrogen gas flow (as per Knudson's U.S. Patent no 4,849.006) was maintained at 0.5L/min to remove volatile Eptam over the study period. Samples were weighted at time intervals and plotted to determine % loss of active. Since no information was provided by Knudson on the methods of loading or experimental designs, we chose a lower flow rate and small volume container to assure proper flushing of active ingredient, and maximum release rates.

#### **Results**

Knudson shows his system to release all of the neat active (without the modified clay) within 6 days. From his loss curves, it is calculated that the Organoclay A+ENDT and organoclay B+ENDT will release all of the active within 12 and 15 days, respectively (Figure 1).

Our comparative data, based of our interpretation of Knudson's limited methods disclosure are provided in Figure 2. As a comparative point of reference for the physical/dynamics of the experimental systems, we can compare the behavior of the

neat active. In our study, we obtain complete depletion in 17 days of the neat active that was applied to filter paper, compared to Knudson's 6 days. While in Knudson's system, depletion of organoclay sorbed active occurs within 12-15 days, our similar nanoclay systems have a depletion rate of 40% of the active lost after 37 days, with a 100% loss time of from about 70 days, using a linear extrapolation method of estimation.

The change in release slope at 12 days (Figure 2) for the nanoclay loaded ENDT/Eptam indicates that the surface/near surface active is releasing rather rapidly compared to the internally absorbed active. This transition is seen to a lesser extent in the Knudson data at 2-3 days. The change (increase) in release slope at 23 days may be due to very low concentration of the active ingredient on the surface when our method of sorption is used.

It would appear that our mixing method, and our physically smaller and organically-modified nanoclays are performing significantly better than that of Knudson. It is clear that release rates can be significantly reduced for highly volatile active trapped in ingredients that are modified intercalated clays.

Our current patent application was intended for the much broader range of bio-actives/pesticides that are not liquid at room temperature, and require melting and mixing of both the active and clays at temperatures above the actives melting point to fully load the active into the nanoclays. Attempts to load solvent saturated actives and/or heated/liquid actives into cooler clays has resulted in the actives condensing onto the outer surface of the clays, or with solvent intercalated systems the evaporation of the solvent actually causes the active to leave the clay by entrainment in the evaporating solvent. The latter results in much lower loading rates in the unheated versus heated systems (<20 versus >40%,w/w). Since we employ these systems as active carriers within a secondary polymeric delivery system, the lack of both internal absorption of the active into the clay, and the presence of active external to the clays, results in much higher release rates, and lower functional longevities, which in our applications frequently must function for 1-30 years.

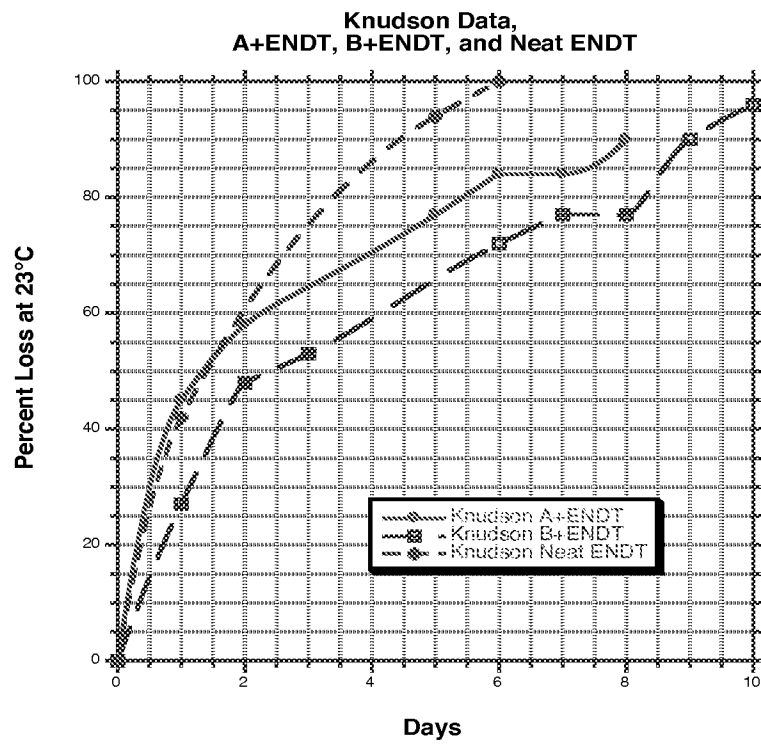


Figure 1: Replot of Knudson Figure 2.

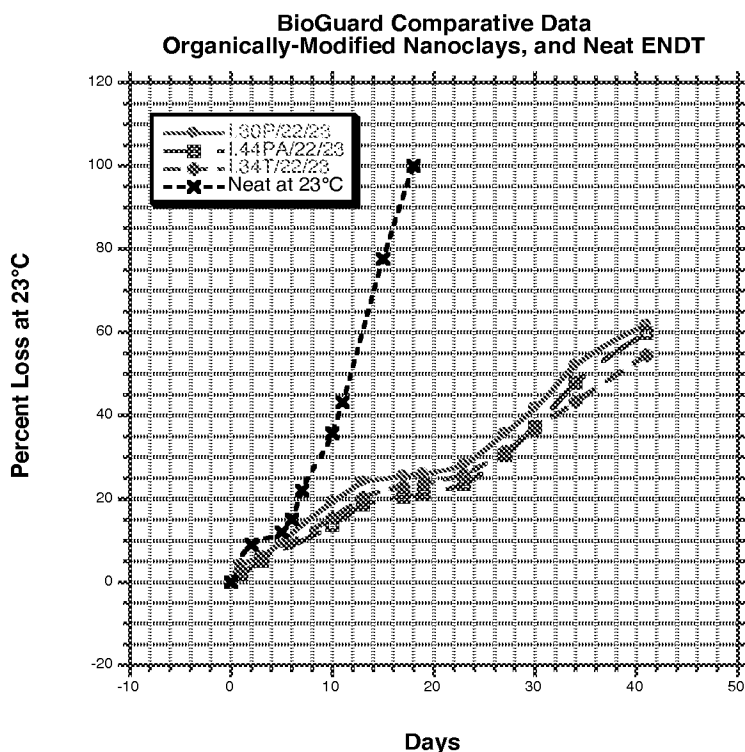


Figure 2: Relative behavior and loss rates for neat ENDT and organically-modified nanoclays of functional longevity

#### Nanoclay Intercalation

When dealing with actives that have higher melting points (*i.e.*, not liquid at room temperature), it is essential to employ mix temperatures, for both the clay and active, 5°-10°C higher than the melting point of the active. In the case of the ENDT/Eptam used by Knudson, it would be expected that use of higher mix temperatures would increase the expansion of the clay plates, and improve intercalation. Figures 3 through 5 show the relative effect of intercalation/active loading at 50° and 22°C, on release rate and longevity of the releasing system.

A close look at the slopes for depletion percent in time clearly show the typical rapid release of surface and near surface active that is not truly intercalated. This is followed by a slowing presumed to be a change in release rate by the intercalated active

ingredient. The I.30P nanoclay shows the most marked slowing in release rate when intercalated at higher temperature.

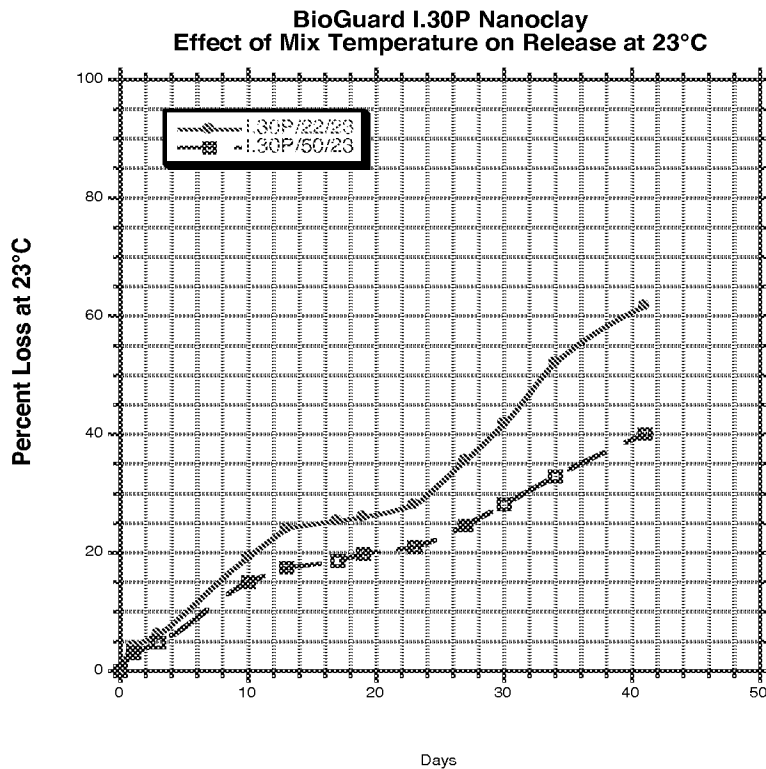


Figure 3: Comparative Release Rate for I.30P Nanoclay intercalated at 22° and 50°C.

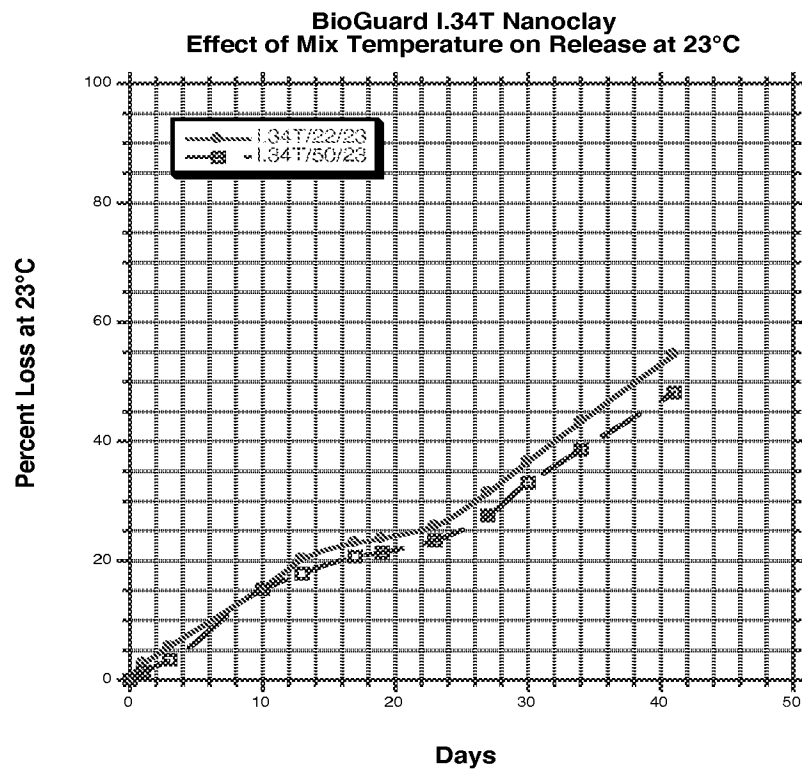


Figure 4: Comparative Release Rate for I.34T Nanoclay intercalated at 22° and 50°C.

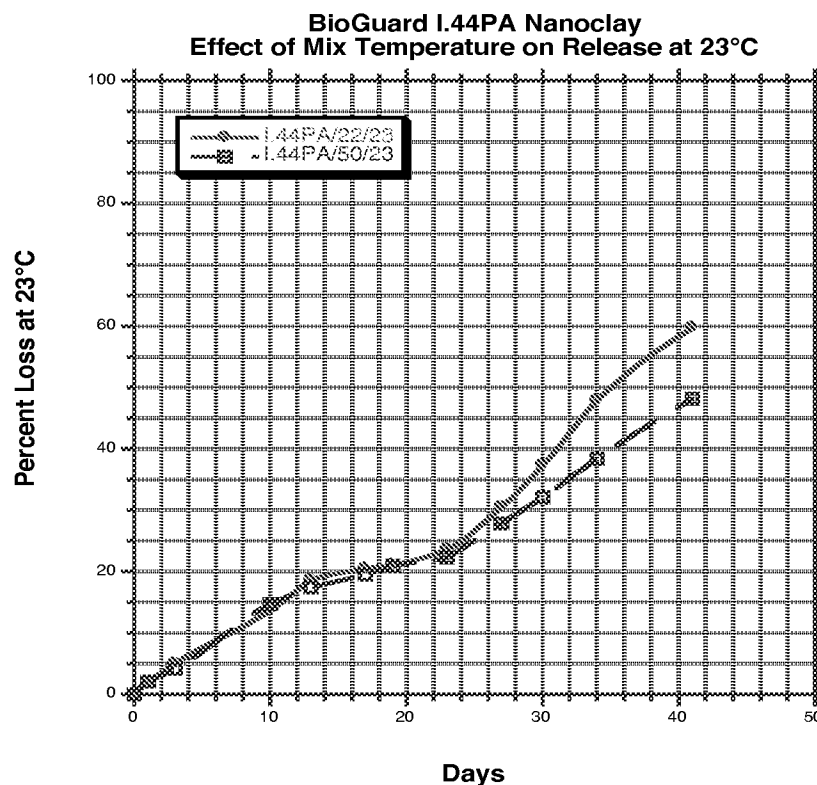


Figure 5: Comparative Release Rate for I.44PA Nanoclay intercalated at 22° and 50°C.

#### **Intercalation of actives that are solids at room temperature**

Our initial efforts centered on creating a nanoclay reservoir/carrier for individual actives to retard release rate, that could then be incorporated into a secondary matrix that would further control/reduce the release rate of actives.

Attempts to intercalate the nanoclays with solvents saturated (20-40%, w/w) with active to bring them to a solution form was less than satisfactory. The use of actives loaded into solvents resulted in a preferential loading of the solvent, and on drying resulted in much of the active actually solvating to the outside of the nanoclay particles; this resulted in a higher release rate of active, than when the actives were thermally intercalated into the nanoclays.



Early attempts to simply mix the heated liquid active heated to above its melting point into the room temperature clays resulted in a similar problem. Under these conditions the active rapidly cools on mixing with the lower temperature clay and fails to allow for intercalation.

The data and results provided for trifluralin, permethrin, lamda-cyhalothrin, cyfluthrin, and other solids (at room temperature) actives clearly follow the same patterns of intercalation. These nanoclay systems can be designed to extend the longevity of both liquid and solid actives, depending on the nature of the active and the required field longevity of the product.

Data Appendix  
Table 1: Release rates for the three sorption phases

Mix Temp/Release Temp (°C)	1-14 Days	25-43 Days	45-63 Days
22/23	0.022	0.027	0.011
50/23	0.018	0.018	0.016

The preceding discussion concerned the cumulative loss of the active ingredient from the loaded product. Now, we examine the release rates. Table 1 provides a summary of the release rates during three time periods. With low temperature mixing of active and clay, the rates over the 60-day period indicate that there is a higher release of the active ingredient that clings to the surface and near surface of the nanoclay particles. At the higher mix temperature, the rates remain relatively constant over the 60-day period. We attribute this constant rate to deep intercalation into the nanoclay with relatively little active ingredient on the surface.

7. Based on this data and my prior research on this invention, I conclude that:
  - (a) These experiments were conducted using the same active ingredient as is used in the examples of U.S. Patent No. 4,849,006 and a variety of organoclays that are within the scope of the above-identified application.
  - (b) U.S. Patent No. 4,849,006 is silent regarding the temperature at which the absorption of the active ingredient into the organoclay occurs. The reported examples imply absorption at ambient temperature. There

certainly is no disclosure or teaching to use other than ambient temperature.

- (c) The present application and thermal experiments show that the release-rate performance of such nanoclay/active ingredient products depend strongly on the temperature at which the liquid pesticide is mixed with the organoclay.
  - (d) The usefulness of these pesticide products is closely related to the number of days in which the active ingredient remains in the end use environment. Our thermal mixing method provides superior longevity.
  - (e) Our cost of attaining a given number of effective days in the environment is lower than that of Knudson due to our need to use less of the ingredients.
  - (f) We have found in many other pesticide experiments that the combination of superior composite materials made from absorption of active ingredient into organoclay is greatly enhanced by their dispersal in specific polymer matrices. U.S. Patent No. 4,849,006 (bottom of column 5 and top of column 6) dismisses this aspect by discussing the formulation of the two ingredients with addition ingredients. We form the sorbed product and only then do we combine this composite material with the specific polymer. We have demonstrated in previous experiments that combining all three is not as good.
8. All statements made herein of our own knowledge are true and all statements made on information and belief are believed to be true, and further that these statements were made with the knowledge that willful false statements and the like so made are punishable by fine or imprisonment, or both, under Section 1001 of Title 18 of the United States Code and that such willful false statements may jeopardize the validity of the application or any patent issuing therefrom.

**FURTHER DECLARANT SAYETH NAUGHT.**



Date: September 28, 2008

Dominic A. Cataldo